II. REMARKS

Claims 1 to 8, 57 and 58 are pending.

A. Regarding the Amendments

The Title has been amended to conform to the claimed subject matter, subsequent to an earlier Restriction Requirement. As such, the amendment merely addresses a formality, and does not add new matter.

Claim 1 has been amended to delete reference to a reporter polypeptide being a polypeptide or epitope that can be bound by an antibody. In addition, claim 1 has been amended to clarify that, "upon cleavage" of the linker polypeptide at the protease cleavage site, "an increase in the activity of said reporter polypeptide can be detected". The amendment is supported, for example, at page 11, lines 24-27, and, therefore, does not add new matter.

Claim 58 has been amended to correct an informality, wherein the term "repressor polypeptide" has been substituted for "inhibitor polypeptide", the latter of which lacks antecedent basis in claim 1, from which claim 58 depends. The amendment is supported, for example, by the language of claim 1, and at page 13, lines 15-19, and, therefore, does not add new matter.

It is submitted that the amendments do not require a new search or consideration because the amendments merely cancel subject matter or clarify the claimed subject matter. The amendments were not made previously because the rejections are newly made in the present Office Action (see, also, Section B, below). The amendments do not add more claims than were finally rejected and, it is submitted, place the claims in condition for allowance, or in better condition for appeal. As such, it is respectfully requested that the amendments be entered.

B. Regarding the Finality of the Office Action

As discussed in Section D., below, the claims are rejected, in part, under 35 U.S.C. § 112, first paragraph. It is stated in the Office Action that the rejections were necessitated by Applicants' previous amendment and, therefore, that the finality of the present Office rejection is proper. In the telephone interview, the Examiner clarified that it was the combination of the "conferring specific localization" and "wherein cleavage increases the activity of the reporter" that was the basis for the finality of the rejection.

As was discussed with the Examiner in the Interview, the previous amendment to claim 1 was based on the acknowledgement in the Office Action mailed June 18, 2002 (Paper No. 18), of the specification "being enabling for a fusion proteins [sic] comprising a repressor polypeptide that confers a specific localization in the cell such that the attached reporter has reduced activity...." (Office Action, page 6, first paragraph). As such, the claims were amended to clarify that the repressor polypeptide "represses the activity of the reporter polypeptide by conferring a specific localization in a cell such that the reporter polypeptide has reduced activity" (see Applicants' Response mailed November 18, 2002). It was also pointed out in the Interview that the term "wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter" was present in the claims as originally filed, and further noted that, in the previous Office Action, the Examiner referred to the reporter as having "reduced activity" due to the specific localization conferred by the repressor.

Because the Examiner stated in the previous Office Action that a repressor polypeptide "confers a specific localization in the cell such that the attached reporter has reduced activity", and because the claims as originally filed recited that "cleavage" of the linker at the protease cleavage site "increases the activity" of the reporter, it is submitted that the present rejections under 35 U.S.C. § 112, first paragraph, could have been made in the previous Office Action, and were not necessitated by Applicants' amendment. Accordingly, it is respectfully requested that, if the present Amendment does not place the claims in condition for allowance, the Examiner

reconsider and withdraw the finality of the present Office Action and issue a further Office Action in this case.

C. Regarding the Drawings

It is stated in the Office Action that the newly submitted drawings are objected to for the reasons set forth on the Form PTO-948 attached to the Action. Applicants have submitted formal Drawings under cover of a separate Communication to Mail Stop PGPUB Drawings and, therefore, respectfully request that this objection be withdrawn. A copy of the formal Drawings is being transmitted herewith for the Examiner's review.

D. Rejections under 35 U.S.C. § 112

The rejections of claims 1 to 8, 57 and 58 under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite are respectfully traversed.

Claim 1, and the claims dependent therefrom, are alleged to be indefinite in that it is unclear with respect to a reporter polypeptide "having an epitope that can be bound by an antibody", wherein the "repressor polypeptide represses the 'activity' of the reporter polypeptide" because all polypeptides have an epitope that can be bound by an antibody and, therefore, the scope of such reporter polypeptides encompasses most polypeptides, and because, if it assumed that the "activity" being referred to is the ability to be bound by an antibody, it is not clear how such an activity can be repressed by conferring a specific localization of the reporter polypeptide in a cell. Although Applicants' traverse this rejection because, for example, a repressor polypeptide can sequester a reporter polypeptide in a cell compartment (e.g., the nucleus), wherein cleavage of the cleavage site allows the reporter polypeptide to translocate to the cell surface, where it can be bound by an antibody, claim 1 nevertheless has been amended to delete reference to a "polypeptide having an epitope that can be bound by an antibody or active antibody fragment" reporter polypeptide in order to advance prosecution of the subject application. Accordingly, it is respectfully requested that this ground of rejection be removed.

It is pointed out in the Office Action that the term "the inhibitor polypeptide" in claim 58 lacks antecedent basis, and suggested that the term should read "the repressor polypeptide". Claim 58 has been amended to correct this informality as suggested by the Examiner. As such, it is respectfully requested that this ground of rejection be removed.

In view of the amendments, it is submitted that one skilled in the art would know the metes and bounds of the claimed invention. Accordingly, it is respectfully requested that the rejections of the claims under 35 U.S.C. § 112, second paragraph, be removed.

The objection to the specification and corresponding rejections of claims 1 to 8, 57 and 58 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description are respectfully traversed.

It is stated in the Office Action that there is no specific example provided of a fusion protein as claimed, wherein "the actual 'cleavage event' at said protease cleavage site increases the activity of said reporter." (Office Action, page 5, first paragraph). As discussed in the Interview, and with reference to the fusion protein exemplified in Figures 1A and 1B, the cleavage event allows the reporter polypeptide, for example, a transcriptional activator that is localized to the cell membrane by the repressor polypeptide, to translocate to the compartment in which it is normally present in a cell (i.e., the nucleus), wherein its transcriptional activity can be detected.

Claim 1 has been amended to clarify that it is not the "actual cleavage event" that increases the activity of the reporter, but that "upon cleavage" of the linker polypeptide at the protease cleavage site, "an increase in the activity of said reporter polypeptide can be detected". The specification discloses such a fusion protein, which comprises a membrane localization domain, a linker containing a variety of protease cleavage sites, and a transcription factor (see Example 1, paragraph bridging pages 30-31; see, also, Figure 1), wherein the intact fusion protein is localized to the cell membrane (Figure 1A) and, upon cleavage at the protease cleavage site, the transactivator reporter polypeptide can translocate to the nucleus and exhibit

transcription activation activity (Figure 1B; see, also, Figures 2 and 3, demonstrating the functionality of the exemplified fusion protein). In addition, the specification discloses several examples of enzyme reporter polypeptides (page 10, lines 6-15) and of repressor polypeptides that direct specific localization in a cell (page 13, line 15, to page 15, line 4), and, it is submitted, additional polypeptides useful as such reporter polypeptides, including transcriptional activators and enzymes, repressors that direct specific localization in a cell, and protease cleavage recognitions sequences would have been well known to the skilled artisan viewing the subject application.

With respect to the objections relating to the aspect of the claims encompassing an epitope reporter polypeptide, the rejection is traversed for the reasons set forth above. Nevertheless, in view of the cancellation of this subject matter from the claims, it is submitted that the issue is moot and, therefore, respectfully requested that this ground of rejection be removed.

For the above reasons, and in view of the amendments, it is submitted that one skilled in the art, viewing the specification, would have known that Applicants were in possession of fusion proteins encompassed within amended claim 1. Accordingly, it is respectfully requested that the objection to the specification be withdrawn, and that the corresponding rejections of claims 1 to 8, 57 and 58 as lacking an adequate written description be removed.

The objection to the specification and corresponding rejections of claims 1 to 22 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed.

It is alleged that specification does not disclose any example of a fusion protein, wherein the reporter polypeptide is activated due to the actual cleavage event and, therefore, that undue experimentation would have been required to make and use such a fusion protein. As discussed above, claim 1 has been amended to clarify that "upon cleavage" of the fusion protein at the protease cleavage site, "an increase in the activity of said reporter polypeptide can be detected". As such, it is submitted that one skilled in the art, viewing the specification, which exemplifies

such a fusion protein (see, for example, paragraph bridging pages 30-31; page 36, line 16, to page 37, line 16; and page 39, line 24, to page 40, line 22; see, also, Figures 1 to 3), and which discloses, for example, additional reporter polypeptides and repressor polypeptides useful for making the claimed fusion proteins, would have known how to make and use the fusion proteins encompassed within the claims, without undue experimentation. Accordingly, it is respectfully requested that this ground of rejection be removed.

With respect to the objections relating to the aspect of the claims encompassing an epitope reporter polypeptide, the rejection is traversed for the reasons set forth above. Nevertheless, in view of the cancellation of this subject matter from the claims, it is submitted that the issue is moot and, therefore, respectfully requested that this ground of rejection be removed.

For the above reasons, it is submitted that the specification enables the fusion proteins encompassed within amended claim 1 such that one skilled in the art would have known how to make and use the claimed compositions without undue experimentation. Accordingly, it is respectfully requested that the objection to the specification be withdrawn, and that the corresponding rejections of claims 1 to 8, 57 and 58 as allegedly lacking enablement be removed.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to the subject application.

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Please charge any additional fees, or made any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: May 27, 2003

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Enclosure: Copy of formal Drawings